SEQ ID NO:2 of the instant application, and as teaching antibodies at columns 23-26. The Office further believes that the antibodies of Ferrara et al. would include antibodies binding to the recited portion of SEQ ID NO:2.

Applicants respectfully traverse this rejection. The rejected claims recite an antibody that specifically binds to an epitope of a polypeptide consisting of a sequence of amino acid residues as shown in SEQ ID NO:2 from residue 235 to residue 345. The disclosure of Ferrara does not teach or suggest an antibody having the recited specificity. Ferrara teaches the use of "the VEGF-E poypeptide or a fusion protein thereof" as an immunogen. See, column 22, lines 66-67 and column 23, lines 22-23. When these statements are read in light of the disclosure at column 4, lines 21-27 and 42-56, one is taught to use as an immunogen a native VEGF-E sequence or "an active VEGF-E polypeptide . . . having at least about 80% amino acid sequence identity with the VEGF-E polypeptide having the deduced amino acid sequence shown in FIG.2 for a full-length native sequence VEGF-E polypeptide." For the reasons discussed below, the use of such an immunogen would not necessarily have produced an antibody as recited in Applicants' claims. Ferrara does not teach or suggest the use, as an immunogen, of a polypeptide consisting of residues 235-345 of Applicants' SEQ ID NO:2 or a peptide fragment thereof. Thus, the claimed antibodies are not disclosed by Ferrara, either explicitly or inherently.

See Col. 16

Enclosed herewith is a Declaration of Christopher Clegg Under 37 C.F.R. § 1.132. As stated by Dr. Clegg, it is likely that the zvegf3 growth factor domain (residues 235-345 of SEQ ID NO:2) is buried within the full-length, precursor form of the protein and becomes exposed only after cleavage between the interdomain region and the growth factor domain. Dr. Clegg thus concludes that if an animal was immunized with a polypeptide comprising at least about 80% of the VEGF-E sequence disclosed by Ferrara et al., one skilled in the art would not reasonably expect to obtain an antibody that specifically binds to an epitope of a polypeptide consisting of a sequence of amino acid residues as shown in Applicants' SEQ ID NO:2 from residue 235 to residue 345.

Li et al. (*Nature Cell Biol.* 2:302-309, 2000) (copy enclosed) also teach that the conformation of full-length PDGF-C (Applicants' zvegf3; Ferrara's VEGF-E) blocks the active region of the molecule:

> Instead the CUB domains are thought to sterically block the receptor-binding epitopes in the unprocessed dimer. This idea is supported by two lines of evidence, from studies of the PDGF-CC core domain and of plasmin-treated full-length PDGF-CC. [Page 307, right column.]

There is thus no reasonable expectation that immunization according to the teachings of Ferrara et al. would result in Applicants' claimed antibodies.

Antibodies raised against full-length zvegf3 at ZymoGenetics, Inc., the assignee of the instant application, did not bind to an epitope of a polypeptide consisting of a sequence of amino acid residues as shown in SEQ ID NO:2 from residue 235 to residue 345. These experiments are described in the enclosed Declaration of Henry Francis Pelto III Under 37 C.F.R. § 1.132. As described in that declaration, Mr. Pelto tested the binding specificity of rabbit polyclonal antisera that was raised against a full-length human zvegf3 protein fused to maltose binding protein. The antisera bound to fused and unfused full-length human zvegf3, but did not bind to isolated human zvegf3 growth factor domain (i.e., residues 235-345 of SEQ ID NO:2), when tested in a Western blot format.

Applicants respectfully submit that the evidence discussed above refutes the Office's assertion that "the antibodies of Ferrara et al. would include antibodies binding to the recited portion of SEQ ID NO:2." Such antibodies are neither explicitly taught by Ferrara nor inherently disclosed. Inherency must be certain. *Ex parte Cyba*, 155 USPQ 756, 757 (Bd. Pat. App. Int. 1966). See also, *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303, 314 (Fed. Cir. 1983) ("Anticipation of inventions set forth in product claims cannot be predicated on mere conjecture respecting the characteristics of products that might result from the practice of processes disclosed in references.") and *Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 63 USPQ2d 1597, 1599 (Fed. Cir. 2002) ("Inherent anticipation requires that the missing descriptive material is 'necessarily present,' not merely probably or possibly present, in the prior art."). Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e) are requested.

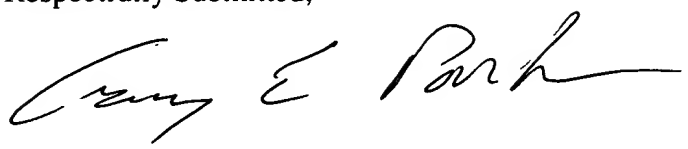
Claim 35 stands rejected under 35 U.S.C. § 103(a). The Office believes the claim is unpatentable over Ferrara et al. in view of Ladner et al., U.S. Patent No. 4,946,778.

Applicants respectfully traverse this rejection. The deficiencies of Ferrara et al. have been discussed above. Ladner et al. does not teach or suggest the preparation of an antibody having the specificity recited in Applicants' claim 35. Thus, the combined references fail to render the claim unpatentable under § 103(a). Reconsideration and withdrawal of the rejection are requested.

On the basis of the above amendments and remarks, Applicants believe that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested. If for any reason the Examiner feels that a telephone conference

would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6673.

Respectfully Submitted,



Gary E. Parker
Registration No. 31,648

Enclosures:

Declaration of Christopher Clegg Under 37 C.F.R. § 1.132
Declaration of Henry Francis Pelto III Under 37 C.F.R. § 1.132
1 Reference
Petition and Fee for Extension of Time (in duplicate)
Amendment Fee Transmittal (in duplicate)
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